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Sulfonamides as Ionophores for Ion-Selective Electrodes. IV. New Secondary Sulfonamide Podands and Cryptands

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Abstract. New compounds – podands and cryptands with two secondary sulfonamide groups – have been synthesized and are described. They were tested as ionophores for guanidinium ions in PVC-membrane electrodes with bis (2-ethylhexyl)sebacate (DOS) as plasticizer.

Key words: Secondary sulfonamides, ion-selective electrodes, ionophores, podands, cryptands, guanidinium ion.

1. Introduction

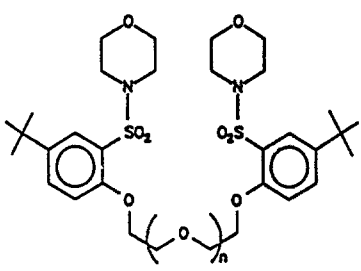
The importance of such derivatives of guanidinium as creatinine, creatine or arginine and methylguanidine in the medical field and in biology explains the reason for the extensive search for sensors for guanidinium ions [1–4]. Hitherto such sensors have been based on crown ethers [1–3] or podands [3, 4]. Some bis-sulfonamido compounds – crown ethers and podands with primary sulfonamido groups – have been found to behave as guanidinium ionophores [4, 5].

Here we present and describe two classes of secondary sulfonamides: open chain podands **1–6** and cryptands **7, 8** shown in Figure 1, and their ionophoric properties in ion-selective electrodes. These compounds do not possess dissociating NH protons and therefore different behaviour might be expected for these ligands than that of the known primary sulfonamides, already studied [4, 5].

We have tested the ionophoric properties of compounds **1–8** and estimated the selectivity coefficients for guanidinium ions over K^+, Na^+, Li^+, Ba^{2+}, Sr^{2+}, Ca^{2+}, Mg^{2+}, Zn^{2+} and Cd^{2+} ions.

2. Experimental

The ^1H NMR spectra were recorded on a Tesla BS 467 spectrometer at 60 MHz in $CDCl_3$ (Aldrich). The mass spectra were obtained on a Varian MAT 711 mass spectrometer using the field desorption technique (FD). Melting points are uncor-



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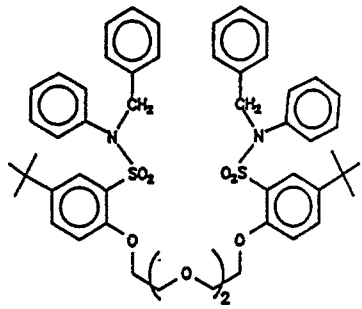

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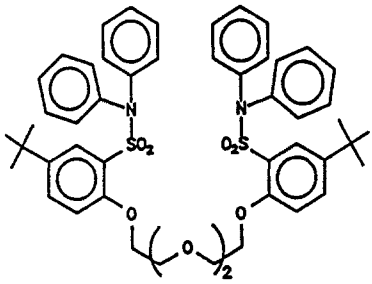

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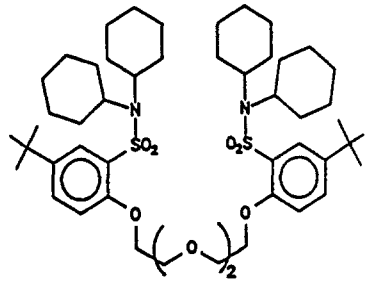

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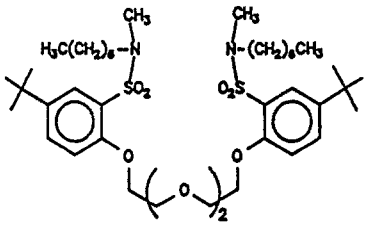

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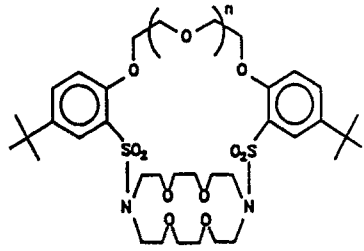

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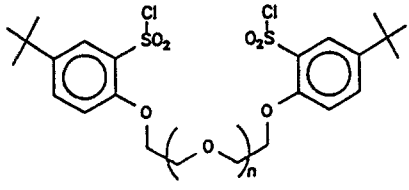
8 n = 2



9 n = 1
10 n = 2

Fig. 1. Compounds in this study.

rected. The ^{1}H NMR spectra and mass spectra of all compounds confirmed their structures and purity.

2.1. SYNTHETIC PROCEDURE

The bis-sulfonamides were prepared starting from bis-sulfonyl chlorides **9** and **10** in a similar way to that described in our earlier publications [6, 7].

2.1.1. *Procedure for the Open Chain Ligands (**1–6**)*

A solution of freshly prepared **9** or **10** (1 mmole) and 4 mmoles of the appropriate secondary amine in dry benzene was refluxed for 24 h. After evaporation of the solvent the mixture was dissolved in methylene chloride, filtered and chromatographed on a silicagel column. The product was eluted with CH_2Cl_2 – acetone (1 : 1) mixture. For better purity it was chromatographed twice.

2.1.2. *Procedure for Bis-sulfonamide Cryptands (High Dilution Method)*

Freshly prepared bis-sulfonyl chloride **9** or **10** (1 mmole) dissolved in 20 mL of DME (1,2-dimethoxyethan) and 1 mmole (262.5 mg) of 1,7,10,16 tetraoxa-4,13-diazacyclooctadecane dissolved in 20 mL of DME were added simultaneously dropwise into a 250 mL flask containing powdered 2 mmoles of sodium or potassium carbonate in 100 mL of DME. The mixture was then refluxed for 48 h. After cooling, the salt was filtered off and the filtrate was evaporated to dryness. The product obtained was chromatographed on a silicagel column (elution with acetone).

2.2. THE ELECTRODE SYSTEM

The poly(vinyl chloride) (PVC) membranes were prepared conventionally, as described in our earlier publications [4]. Bis(2-ethylhexyl) sebacate (DOS) was used as plasticizer. The PVC membranes were incorporated into Ag/AgCl electrode bodies with 0.01 M KCl solution as internal electrolyte. A double junction reference electrode (OP 082OP, Radelkis) was used with a 0.1 M CH_3COOLi solution in the bridge cell.

2.2.1. *EMF Measurements*

All potentials were measured at 20°C using a 654 (Metrohm) pH meter, allowing a reading accuracy up to 0.1 mV.

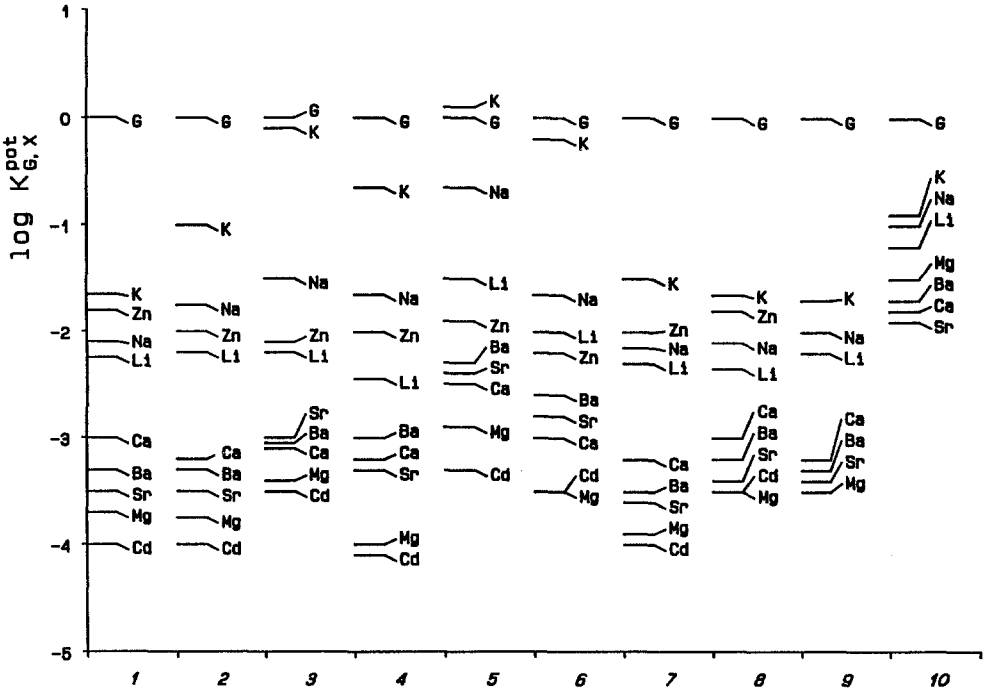


Fig. 2. The selectivity coefficients for electrodes **1–10**.

3. Results and Conclusions

The yields and physical properties of the synthesized compounds are given in Table I. They were all obtained as white crystals.

The properties of the electrodes **1–10** (the slopes and linear ranges for guanidinium ions) with the membranes containing sulfonamides as ionophores and bis(2-ethylhexyl) sebacate (DOS) as plasticizer are summarized in Table II. The characteristics of the electrodes were satisfactory only after the addition of a lipophilic salt, potassium tetrakis(4-chlorophenyl)borate (KpClPB) to the membrane composition. The anionic site probably acts as a catalyst for ion transfer from the sample solution to the membrane phase. The selectivity coefficients for the electrodes **1–10**, expressed as log $K_{G,M}$, where M = K^+, Na^+, Li^+, Ba^{2+}, Sr^{2+}, Ca^{2+}, Mg^{2+}, Zn^{2+} and Cd^{2+} are shown in diagram form in Figure 2. They were determined by the separate solution method (SSM), at 0.1 M concentration.

Most of the compounds studied show preference for the large monovalent guanidinium cation and the selectivity pattern is in all cases similar: $G^+ > K^+ > Na^+ > Li^+$.

The lipophilicities (log P) of the compounds studied, the morpholides **1–2** and crytands **7–8** are smaller (calculated according to the method of Hansch [8] log P = 4.6–5.2) than those for the previously studied primary sulfonamides (log P = 8.5–10.4) [4]. In contrast to this, the lipophilicities of podands **3–6** are higher (calculated

TABLE I. Properties of compounds **1–8**.

Compound	Formula	FD M^+	Yield [%]	m.p. [°C]	^{1} NMR spectra (δ) [ppm]
1	$C_{32}H_{48}O_9S_2N_2$	668	75	189–190	1.25 (s,18H), 3.15 (m,8H), 3.65 (m,8H), 3.9 (m,4H), 4.1 (m,4H), 6.85 (d,2H), 7.35 (d,2H), 7.8 (2s,2H)
2	$C_{34}H_{52}O_{10}S_2N_2$	712	50	142–143	1.25 (s,18H), 3.2 (m,8H), 3.6 (s,4H), 3.65 (m,8H), 3.85 (m,4H), 4.15 (m,4H), 6.8 (d,2H), 7.3 (d,2H), 7.75 (s,1H), 7.8 (s,1H)
3	$C_{54}H_{64}O_8S_2N_2$	932	45	102–106	1.26 (s,18H), 3.33 (s,4H), 3.6 (m,4H), 4.0 (m,4H), 4.36 (s,8H), 6.84 (d,2H), 7.1 (s,20H), 7.5 (d,2H), 7.92 (s,2H)
4	$C_{52}H_{60}O_8S_2N_2$	904	30	108–110	1.16 (s,18H), 3.58 (s,4H), 3.84 (d,4H), 4.1 (d,4H), 5.0 (s,4H), 6.84 (m,4H), 7.05 (s,10H), 7.25 (s,10H), 7.4 (d,2H), 7.6 (s,2H)
5	$C_{50}H_{80}O_8S_2N_2$	900	25	172–174	1.28 (s,18H), 1.66 (m,40H), 3.4 (m,4H), 3.73 (s,4H), 3.95 (d,4H), 4.15 (d,4H), 6.9 (d,2H), 7.35 (d,2H), 7.87 (2s,2H)
6	$C_{42}H_{72}O_8S_2N_2$	796	30	106–108	0.8 (t,6H), 1.25 (s,m,36H), 2.8 (s,6H), 3.05 (m,4H), 3.65 (s,4H), 3.9 (m,4H), 4.15 (m,4H), 6.9 (d,2H), 7.35 (d,2H), 7.8 (s,1H), 7.88 (s,1H)
7	$C_{36}H_{56}O_{11}S_2N_2$	756	65	182–184	1.25 (s,18H), 3.45 (m,24H), 3.95 (d,4H), 4.1 (d,4H), 6.8 (d,2H), 7.3 (d,2H), 7.75 (s,1H), 7.8 (s,1H)
8	$C_{38}H_{60}O_{12}S_2N_2$	800	22.5	211–212	1.27 (s,18H), 3.3–3.7 (m,28H), 3.9 (m,4H), 4.15 (m,4H), 6.85 (d,2H), 7.33 (d,2H), 7.8 (s,2H)

TABLE II. PVC membrane composition and characteristics of the electrodes **1–10**.

Electrode	PVC membrane composition			Electrode characteristic		Selectivity
	ionophore	plastic	KTpClPB[a]	S^d_{G+} [mV]	linear range [-log c_G]	log $K_{G,K}$
1	**1**	DOS	5 M%	58	5.5–1	-1.65
2	**2**	DOS	5 M%	53	5.0–1	-1.00
3	**3**	DOS	5 M%	52	4.8–1	-0.10
4	**4**	DOS	5 M%	55	4.8–1	-0.65
5	**5**	DOS	5 M%	60	5.4–1	0.10
6	**6**	DOS	5 M%	53	4.5–1	-0.20
7	**7**	DOS	5 M%	50	4.8–1	-1.50
8	**8**	DOS	5 M%	50	4.8–1	-1.65
9	–	DOS	+[b]	53	4.8–1	-1.65
10	–	DOS	–[c]	37	4.0–1	-0.90

[a] M% = mole% amount of borate against ionophore.

[b] Blank membrane with similar amount of KTpClPB (1 mg).

[c] Blank membrane without borate.

[d] Slope of the characteristic for guanidinium ion.

log P = 11.5–15.2) and therefore an increased membrane lifetime with these ionophores has to be expected; but then, the bulky substituents on the nitrogen atoms might prevent the molecule from adopting a suitable conformation for complexation and worse guanidinium selectivity with electrodes **3–6** is observed.

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